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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,808	09/22/2004	Robert J. Etches	700603.7/1	3921

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	**PAPER NUMBER**
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,808	ETCHES ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9-22-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendments to the claims

Claims 10-19 have not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified. Note: the status of every claim must be indicated after its claim number by one of the following status identifiers: (Original), (Currently amended), (Canceled), (Previously presented), (New), (Not entered), (Withdrawn) and (Withdrawn-currently amended). The text of withdrawn or canceled claims (claims 1-9 and 20, for example) need not be repeated. In order to expedite prosecution, claims 10-19 are being treated as "(Orignal)" claims.

Claims 1-9 and 20 have been canceled. Claims 10-19 are pending and under consideration.

Election/Restrictions

Applicant's election of Group II, claims 10-19, in the reply filed on 10-18-06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or

Amino Acid Sequence Disclosures. **The sequences throughout the specification do not include SEQ ID NOs. See pg 32, lines 1-5; pg 35, lines 10-11, pg 36, lines 8-9; pg 42, lines 6-9; pg 42, lines 16-24; pg 43, line 1; pg 43, lines 16-20**. Applicants must file a "Sequence Listing" accompanied by directions to enter the listing into the specification as an amendment. Applicant also must provide statements regarding sameness and new matter with regards to the CRF and the "Sequence Listing." Failure to fully comply with the sequence rules in response to the instant office action will be considered non-responsive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic chicken whose genome comprises a variable and joining region of a heavy or light chain human immunoglobulin gene, does not reasonably provide enablement for making a transgenic chicken expressing human variable and joining regions of a heavy or light chain immunoglobulin gene under the control of an endogenous B cell specific regulatory region. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claim and its breadth

Claim 19 is drawn to a transgenic chicken that expresses human variable and joining regions of a heavy or light chain immunoglobulin under the control of a B cell specific regulatory region. The specification discusses using an endogenous chicken promoter "for expression in B cells" (pg 48, lines 19-26; pg 49, lines 4-8). Thus, claim 19 is limited to a transgenic chicken expressing human variable and joining regions of a heavy or light chain immunoglobulin under the control of an endogenous B cell specific regulatory region. However, the specification does not provide adequate guidance that the knockout construct will be stably integrated into the genome such that a knockout chicken occurs or that the human immunoglobulin genes are operably linked to the endogenous B cell promoter.

State of the art and level of skill

Knockout mice were known at the time of filing. Jakobovits (US Patent 5,998,209, 12-7-99), Ginsburg (US Patent 6,066,778, 5-23-00) and Kucherlapati (US Patent 5,939,598, 8-17-99) made knock-in mice having human immunoglobulin genes. The art at the time of filing taught the method required transfecting mouse ES cells with a knockout construct, culturing the cells over a period of time, selecting the ES cells having the desired knockout and implanting the ES cells into a recipient embryo. See, for example, Kucherlapati who selected mouse ES cells having the desired knockout, which was essential to make a mouse having an immunoglobulin gene knockout (col. 10, line 47). However, the ability to make knockout mice is no indication that knockout

avians are enabled because attempts to make knockout avians have failed as will be discussed below.

The art at the time of filing contemplated knockout chickens but did not teach the essential means to stably transfect avian ES cell over a period of time such that a knockout transgenic chicken was made.

Stage XI PGCs had been isolated from chickens, transduced with retrovirus, and immediately injected into the vasculature of Stage 15 chick embryos to obtain germline transmission of a transgene (Vick, Proc. R. Soc. Lond., 1993, Vol. 251, pg 179-182). Plasmid DNA had been injected into the germinal disc of chick zygotes isolated before being laid to obtain germline transmission of a transgene (Love, Bio/Technology, 1994, Vol. 12, pg 60-63). Retroviral vectors had been injected into the subgerminal cavity of an avian embryo in a freshly laid egg to obtain germline transmission of a transgene (Thoroval, Transgenic Research, 1995, Vol. 4, pg 369-376). Retroviral vectors had been used to introduce a truncated antibody receptor into chickens "somatically" and express the receptor in the bursa at hatch (Sayegh, Dec. 15, 1999, Vol. 72, pg 31-37; pg 32, 2nd full para., lines 2-5 and 16-18; para. bridging pg 33-34).

Pain (1996, Development, Vol. 122, pg 2339-2348) taught culturing chicken ES cells over a period of time, but did not teach transfecting the ES cells and maintaining the ES cells over that period of time.

Mohammed (1998, Immunotechnology, Vol. 4, pg 115-125) taught that although using hens for the production of recombinant human antibodies (rhAb) has been discussed, it has never been demonstrated. Mohammed transfected a lymphoblastoid

cell line with a retrovirus encoding a rhAb, injected the cells into a chicken and obtained expression of the rhAb in the egg yolk and sometimes the egg white (pg 116, col. 1, 2nd ¶; col. 2, 1st full ¶). Mohammed suggested suppressing the expression of endogenous chicken Ig but did not teach how to inactivate a gene in an avian (pg 124, col. 2, 2nd ¶, line 9) and did not teach how to obtain a transgenic avian having an inactivated immunoglobulin gene. The transfected lymphoblastoid cell line (DT40) maintained in culture for two days used by Mohammed to obtain antibodies in the egg cannot be used to disrupt chicken heavy chain immunoglobulin gene in a knockout chicken because the transfected chicken DT40 cells are differentiated cells that cannot be used to make a knockout chicken. The method of Mohammed is not a method of disrupting a chicken gene in a transgenic chicken because the transfected cells cannot integrate into the germline of a chicken, which is essential to make a knockout chicken.

Fukagawa (Nucleic Acids Res. 1999, Vol. 27. pg 1966-1969) taught making a "knockout" construct that disrupted the chicken HPRT gene in DT40 cells that required Cre recombinase (¶ bridging pg 1966-1967).

Since the time of filing, Ishida (2002, Cloning Stem Cells, Vol. 4, pg 91-102) suggested making chickens expressing human antibodies but did not teach how to make transgenic chickens or how to inactivate chicken genes (see abstract).

Ivarie (Trends in Biotechnology, Jan. 2003, Vol. 21, pg 14-19) taught that because of the complex process by which a bird makes and lays eggs, transgenic procedures for birds have lagged far behind those of other organisms. Ivarie cites Pain who taught long-term culture of non-transfected, blastodermal cells that provided

germline transmission; however, no transgenic birds have been made using transfected ES cells or PGCs. The biggest obstacle to overcome in making transgenic birds using transfected ES cells or PGCs is the loss of germline competence during culture of transfected ES cells and PGCs (pg 14, col. 2, 3rd full ¶, 1st sentence; pg 17, col. 1, 2nd full ¶, last two sentences; pg 17, sentence bridging col. 1-2; pg 17, col. 2, last sentence).

Thus, the state of the art at the time of filing was that "knockout" constructs had not been stably transfected into chicken ES cells or PGCs such that "knockout" chickens having a disruption in a chicken gene had been obtained because the transfected chicken ES cells or PGCs could not be cultured over an adequate period of time while maintaining the ES cell or PGC phenotype and integrating the "knockout" construct.

Teachings in the specification

The specification suggested inactivating the immunoglobulin genes in chickens in Example 1 (pg 34) and describes constructs comprising genomic chicken immunoglobulin sequences; however, the specification does not teach the constructs knockout chicken immunoglobulin genes in vitro or in vivo.

The specification suggests using a construct comprising a telomere to eliminate an endogenous immunoglobulin heavy chain gene (Example 3, pg 37). The specification does not adequately describe the structure of the construct so that the endogenous gene would be knocked out. It cannot be envisioned how the telomere overcomes the unpredictability in the art regarding how to knockout a gene in a chicken.

The specification suggests modifying chromosome 15 with a recombination site centromeric of the endogenous immunoglobulin gene such that deletion of all the DNA telomeric of the site renders the chicken immunoglobulin non-functional. Subsequently, a construct containing a complimentary recombination site attached to exogenous DNA comprising a human immunoglobulin gene is inserted into the cell (Example 4, pg 38). The example is prophetic and does not provide the specific structure of the knockout construct having the ability to knockout a chicken immunoglobulin gene. The addition of recombination sites and a telomere into the construct as described prophetically in Example 4 is not adequate to indicate chicken ES cells or PGCs transfected with the construct would be cultured over an adequate period of time while maintaining the ES cell or PGC phenotype and integrating the "knockout" construct.

Likewise, the specification suggests transferring chromosome 15 into ES cells such that deletion of the chicken immunoglobulin gene occurs (Example 5, pg 40). The example is prophetic and does not provide the specific structure of the chromosome having the ability to knockout a chicken immunoglobulin gene. The addition of a chromosome as described prophetically in Example 5 is not adequate to obtain the normal number of chromosomes or that chicken ES cells receiving the donor chromosome would be cultured over an adequate period of time while maintaining the ES cell or PGC phenotype and integrating the "knockout" chromosome such that the knockout is maintained.

Example 6 teaches making a BAC construct comprising human immunoglobulin genes (pg 42) but does not teach the BAC construct is able to stably transfect chicken

ES cells or PGCs such that the cells would be cultured over an adequate period of time while maintaining the ES cell or PGC phenotype and integrating the "knockout" construct.

Example 7 discusses rearrangement as mentioned in claim 16 but does not indicate the construct will stably transfect chicken ES cells or PGCs such that the cells would be cultured over an adequate period of time while maintaining the ES cell or PGC phenotype and integrating the "knockout" construct. Nor does example 7 provide adequate guidance for those of skill to determine the structure of the construct required to rearrange immunoglobulin genes to yield isotype G immunoglobulin genes as claimed (pg 16). Without such guidance, it would require those of skill undue experimentation to determine the structure of the construct in Example 7 required to rearrange immunoglobulin gene to yield isotype G immunoglobulin molecules as claimed.

Examples 8 and 9 describe a human kappa light chain transgene and do not relate to knocking out an endogenous immunoglobulin gene.

Amount of experimentation

All of the examples in the specification require stably transfecting ES cells such that the cells maintain the ES cell phenotype and stably incorporate the transgene. Applicants have not overcome the art established unpredictability in the art by providing adequate guidance that recombination sites (Example 4, pg 38, lines 9-12), chromosome transfers (Example 5, pg 40) or BAC vectors (Example 6, pg 41) cause stable transfection of ES cells such that the ES cells maintain the ES cell phenotype.

None of the examples described how to overcome this art established problem. Without such guidance, it would require one of skill undue experimentation to obtain a transgenic chicken expressing human variable and joining regions of a heavy or light chain immunoglobulin under the control of an endogenous B cell specific regulatory region as claimed.

Conclusion

The specification does not overcome the art established unpredictability for those of skill to determine the parameters required to the culture transfected chicken ES cells or PGCs over an adequate period of time while maintaining the ES cell or PGC phenotype and integrating the "knockout" construct. Thus, the specification does not enable making a transgenic chicken expressing human variable and joining regions of a heavy or light chain immunoglobulin under the control of an endogenous B cell specific regulatory region as claimed.

Written Description

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

An adequate written description of a B cell specific regulatory region requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the regulatory region itself. It

is not sufficient to define a regulatory region solely by its principal biological property, i.e. being specific to B cells, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any regulatory region with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all regulatory regions that are specific to B cells without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

Indefiniteness

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite because the phrase "wherein a population of B lymphocytes of the chicken are a human immunoglobulin locus encoding a human immunoglobulin heavy or light chain immunoglobulin molecule" is unclear. A B cell can comprise a human gene but cannot comprise a human chromosome position as claimed.

The phrase "pseudo" in claims 15 and 18 is indefinite. It cannot be determined how "like" a human heavy chain V region a gene must be to be a "pseudo V gene" for example.

Claim 16 is indefinite because the structure of the resulting IgG molecule after switching cannot be determined. In addition, it cannot be determine what applicants consider "class switching." The distinction between rearrangement and switching cannot be determined. Ultimately, the structure of the "isotype G immunoglobulin molecules" in the B-cells cannot be determined.

The metes and bounds of what applicants consider a "B lymphocyte specific regulatory region" (claim 19). The specification and the art at the time of filing do not define such regulatory regions. Furthermore, the specification states the human immunoglobulin gene is operably linked to an endogenous chicken regulatory region; however, that structure is not evident from claim 19 as written.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Rapp (Patent Application Publication US 2002/0108132 A1).

Rapp taught a transgenic chicken whose genome comprised a transgene encoding a human heavy and/or light chain antibody comprising the V, D, C and J regions (paragraphs 63, 76, 151, 154, 161, 163).

The phrase "wherein a population of B lymphocytes of the chicken are a human immunoglobulin locus" in claim 10 does not make sense because B lymphocytes cannot comprise a locus as claimed. A locus is a position on a chromosome; thus, a B-cell cannot comprise a position as claimed (see 112/2nd). It is noted that if the phrase is intended to mean the B-cells comprise a human immunoglobulin coding sequence, the B-cells of Rapp inherently comprise a human immunoglobulin coding sequence because the transgene encoding the human immunoglobulin is part of the chicken's genome (paragraph 76).

If claims 10 or 19 are intended to limit the transgenic chicken to a knock-in transgenic chicken (see 112/2nd), Rapp described making a knock-in transgenic chicken in paragraphs 80 and 121.

Claims 12-15 and 18 are included because the transgene may comprise a plurality of heavy or light chain V or D regions (paragraph 154). Claims 15 and 18 are included because the human immunoglobulin transgene is "like" the chicken immunoglobulin gene, i.e. "pseudo". The instant application does not define pseudo genes, thus leaving the meaning open to any reasonable interpretation.

Claim 16 is included because the B cells of the chicken inherently undergo immunoglobulin gene rearrangement class switching and yield isotype G immunoglobulin molecules because the transgene of Rapp encoded an entire heavy or

light immunoglobulin chain that inherently comprised the switch region. Without evidence to the contrary, the transgene taught by Rapp has the function of claim 16. The structure of the transgenic chicken in claim 16 is not distinguished over the structure of the transgenic chicken described by Rapp.

Claim 17 is included because the antibody was expressed in the yolk of an egg produced by the chicken (paragraph 108).

Claim 18 is included because Rapp used the CMV promoter to express the transgene, which inherently expressed the transgene in all tissues, specifically in B-lymphocytes as claimed. The structure of the "B lymphocyte specific regulatory region" in claim 18 is not distinguished by structure or function over the CMV promoter described by Rapp.

Claims 10-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Buelow (US Patent 7129084).

Buelow taught a vector encoding human variable, joining and diversity immunoglobulin genes capable of replacing endogenous immunoglobulin variable, joining and diversity regions. Specifically Buelow taught a BAC vector with a chicken light chain modified by homologous recombination (Fig. 13-15). The vectors are used to make knock-in chickens expressing human variable and joining regions of an immunoglobulin gene (Examples 12-14). The vectors inherently comprise B cell specific regulatory regions operably linked to the human immunoglobulin gene (claim 19) because they are linked to the endogenous chicken heavy chain gene (col. 26, Example 11).

Claims 10-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Singh (US Patent Application Publication 2002/0028488).

Singh taught a vector encoding human variable, joining and diversity immunoglobulin genes capable of replacing endogenous immunoglobulin variable, joining and diversity regions. Specifically Singh taught a vector with a chicken light and heavy chain modified by homologous recombination (Fig. 2-4). The vectors are used to make knock-in chickens expressing human variable and joining regions of an immunoglobulin gene. The vectors inherently comprise B cell specific regulatory regions operably linked to the human immunoglobulin gene (claim 19) because they are linked to the endogenous chicken heavy or light chain gene (pg 8, paragraph 84).

Claims 10-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Etches (US Patent 6,861,572).

The applied reference has common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Etches taught a transgenic chicken whose genome comprises a transgene encoding a human variable, diversity and joining regions of a human heavy or light chain immunoglobulin as claimed. The structure of the chicken claimed in this application is obvious in view of the disclosure of '572.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 10-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 11/062325.

Claim 8-11 of '325 are drawn to a genetically modified chicken expressing in tubular gland cells monoclonal antibodies encoded by an exogenous polynucleotide, wherein the monoclonal antibodies are present in egg white at a concentration of at least 40 .mu.g/ml. The product claimed in '325 is an obvious variant of the product claimed in the instant application and is described in the instant disclosure. The product claimed in this application is obvious in view of the claims of '089 taken with the disclosure of '089. This is a provisional obviousness-type double patenting rejection.

Claims 10-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 10/524089.

Claim 1-8 of '089 are drawn to A chicken selectively expressing exogenous protein in tubular gland cells wherein the protein is encoded by a transgene stably integrated into a genome of the chicken and wherein the transgene is comprised at least a portion of a promoter of a gene encoding an egg white protein that is operably linked to DNA encoding the exogenous protein. The product claimed in '089 is an obvious variant of the product claimed in the instant application and is described in the disclosure of '089. The product claimed in this application is obvious in view of the claims of '089 taken with the disclosure of '089. This is a provisional obviousness-type double patenting rejection.

Claims 10-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9-10 of copending Application No. 10/216098.

Claim 9-10 of '098 are drawn to a chimeric chicken selectively expressing exogenous protein in tubular gland cells, wherein the exogenous protein is encoded by a transgene stably integrated into a genome of a donor embryonic stem cell whose progeny contribute to the chimeric chicken, and wherein the transgene is greater than 15 kb in size and is comprised of an at least a 7.5 kb portion of an ovalbumin promoter operably linked to DNA encoding the exogenous protein. The product claimed in '098 is an obvious variant of the product claimed in the instant application and is described in

the disclosure of '098. The product claimed in this application is obvious in view of the claims of '098 taken with the disclosure of '098. This is a provisional obviousness-type double patenting rejection.

Claims 10-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7 and 9 of US Patent 6,861,572.

Claim 1, 7 and 9 of '572 are drawn to an egg-laying chicken whose somatic cells contain an expression system comprising (i) a first DNA sequence encoding a human gamma isotype immunoglobulin constant region having a CH2-CH3 region in an Fc domain of the constant region; (ii) a second DNA sequence encoding a human immunoglobulin variable region; (iii) a third DNA sequence comprising an immunoglobulin-gene derived promoter sufficient for expression of the human immunoglobulin constant region in the chicken; wherein the egg-laying chicken produces eggs whose yolk contains human gamma isotype immunoglobulin having a constant region encoded by the first DNA sequence and a variable region encoded by the second DNA sequence. The product claimed in '572 is an obvious variant of the product claimed in the instant application and is described in the disclosure of '572. The product claimed in this application is obvious in view of the claims of '572 taken with the disclosure of '572.

Claim 12 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 14. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is

proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

MacArthur (WO 97/47739)

MacArthur (US Patent 6,825,396, Nov. 30, 2004, filed 4-18-97)

Davis (Bio/Technology, Feb. 1991, Vol. 9, pg 165-169)

Etches, US Patent Application 10/067148 now US Patent 7,145,057.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER